

NDA 16-016/S-070

AUG 22 1999

Merck & Co.
Attention: Larry P. Bell, M.D.
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Bell:

Please refer to your supplemental new drug application dated May 12, 1999 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aldoclor (methyldopa/chlorothiazide) Tablets.

We note that this supplement was submitted as a 'Special Supplement - Changes Being Effectuated' under 21 CFR 314.70(c).

This supplemental new drug application provides for final printed labeling revised under **PRECAUTIONS**, *Drug Interactions*, *Methyldopa* to include a statement regarding drug interaction between methyldopa and ferrous sulfate or ferrous gluconate. A statement regarding drug interaction between methyldopa and lithium was also added. These statements are consistent with that in the Aldomet Tablets labeling. Your submission stated January 1, 2000 as the implementation date for these changes.

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the final printed labeling included in your May 12, 1999 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

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If you have any questions, please contact:

Mr. David Roeder
Regulatory Health Project Manager
(301) 594-5313.

Sincerely,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Drug Interactions Methyldopa

When methyldopa is used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Patients may require reduced doses of anesthetics when on methyldopa. If hypotension does occur during anesthesia, it usually can be controlled by vasopressors. The adrenergic receptors remain sensitive during treatment with methyldopa.

When methyldopa and lithium are given concomitantly the patient should be carefully monitored for symptoms of lithium toxicity. Read the prescribing information for lithium preparations.

Several studies demonstrate a decrease in the bioavailability of methyldopa when it is ingested with ferrous sulfate or ferrous gluconate. This may adversely affect blood pressure control in patients treated with methyldopa. Coadministration of methyldopa with ferrous sulfate or ferrous gluconate is not recommended.

Monoamine oxidase (MAO) inhibitors: See CONTRAINDICATIONS.